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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,803	01/14/2004	James McSwiggen	SIR-MIS-00001-US-CIP[4]	5421
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Sirna Therapeutics, Inc. 1700 Owens Street 4th Floor San Francisco, CA 94158			EXAMINER BOWMAN, AMY HUDSON	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 01/22/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/757,803

Applicant(s)

MCSWIGGEN ET AL.

Examiner

AMY BOWMAN

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-20 and 33-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-20 and 33-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 12/26/08 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 7/2/08 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/26/08 has been entered.

Claims 18-20 and 33-38 are pending in the application.

Applicant's arguments filed on 12/26/08, with respect to the Double Patenting rejections (except for 10/923,536), have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, the Double Patenting rejection (10/923,536) and the rejection under 35 USC 103(a) are pending as explained below.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) or 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The instant claims are accorded the priority date of 2/20/2002, which is the filing date of application 60/358,580, because application PCT/US03/05346 and application 60/358,580 are the earliest-filed applications that teach each of the limitations of claims 18-20 and 33-38.

Response to Arguments--Claim Rejections - 35 USC § 103

Claims 18-20 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir et al. (The EMBO Journal, 2001, Vol. 20, No. 23, pages 6877-6888), in view of Matulic-Adamic et al. (US 5,998,203), Parrish et al. (Molecular Cell, Vol. 6, pages 1077-1087, 2000), and Crooke (US 5,898,031), for the reasons of

record set forth in the office action mailed on 12/21/06, the advisory actions mailed on 3/27/07 and 5/1/07, the office actions mailed on 10/30/07 and 7/2/08, and as explained below.

It is noted that the references are of record and cited on the PTO-892 mailed on 12/21/06.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The invention of the above claims is drawn to a chemically modified double stranded nucleic acid comprising a sense strand and an antisense strand, wherein each strand is 18 to 27 nucleotides in length, 18 to 23 nucleotides of each strand are

complementary to each other, and at least 18 nucleotides of the antisense strand are complementary to a target RNA sequence, and the sense strand comprises a terminal cap moiety at the 5' and 3' end and the antisense strand optionally includes a terminal cap moiety at the 3' end. The invention is further drawn to specific terminal cap moieties, as well as modifications to the duplex and a composition comprising the double stranded nucleic acid and a pharmaceutically acceptable carrier or diluent.

Elbashir et al. (EMBO) teach siRNAs, wherein each strand is 21-23 nucleotides in length and wherein at least 19 nucleotides of the sense strand are complementary to the antisense strand. Elbashir et al. teach chemical modification with 2'-deoxy or 2'-O-methyl modifications. Elbashir et al. teach modification of 19% of the nucleotides of a duplex 21 nucleotides in length with 2'-deoxy modifications.

Elbashir et al. teach duplexes with 2 nt 3' overhangs, as well as blunt ended duplexes wherein all 21 nucleotides are complementary between the sense and antisense strand. Elbashir et al. teach that duplexes 21 nucleotides in length with 2 nt 3' overhangs were the most efficient triggers of sequence-specific mRNA degradation. Elbashir et al. teach duplexes wherein the sense and antisense strands are complementary at 19 or 21 nucleotide positions (see for example, Figure 1D (1st duplex) and Figure 1F (1st duplex)). Elbashir et al. teach 2'-deoxythymidine in the 3' overhang (see page 6884). The 100% modified duplex taught by Elbashir et al. is considered to not comprise ribonucleotides.

Elbashir et al. do not teach double stranded nucleic acid molecules comprising the instantly recited terminal cap moieties and do not teach 2'-deoxy-2'-fluoro

modifications. Elbashir et al. do not teach a composition comprising the double stranded nucleic acid molecule and a pharmaceutically acceptable carrier.

Matulic-Adamic et al. teach chemical modifications of double stranded nucleic acid structures. The enzymatic RNA molecules of Matulic-Adamic et al. are taught to be targeted to virtually any RNA transcript and achieve efficient cleavage (see column 1) and to be sufficiently complementary to a target sequence to allow cleavage. Matulic-Adamic et al. teach the incorporation of chemical modifications at the 5' and/or 3' ends of the nucleic acids to protect the enzymatic nucleic acids from exonuclease degradation, which improves the overall effectiveness of the nucleic acid, as well as facilitates uptake of the nucleic acid molecules (see column 2). Matulic-Adamic et al. teach base, sugar and/or phosphate modification, as well as terminal cap moieties at the 5'-cap, 3'-cap, or both. Specifically, 3' phosphorothioates, inverted abasic moieties, and 2'-O-methyl modifications are utilized. Matulic-Adamic et al. teach 2'-deoxy nucleotides and 2'-deoxy-2'-halogen nucleotides, wherein Br, Cl and F are representative halogens (see column 3, for example). For example, figure 3 contains a ribozyme structure that encompasses modification of at least 20%, at least 30%, at least 40% or at least 50% of the nucleotide positions, as well as the modifications instantly claimed. The modifications can be in one or both of the strands and can be modifications of different types within the same structure.

Matulic-Adamic et al. teach that preferred caps include 4', 5'-methylene nucleotides, 1-(beta-D-erythrofuransyl) nucleotides, 4'-thio nucleotides, 1,5-anhydrohexitol nucleotides, L-nucleotides, threo-pentofuransyl nucleotides, acyclic 3',

4'-seco nucleotides, 3,4-dihydroxybutyl nucleotides, 3,5-dihydroxypentyl nucleotides, 3'-3'-inverted nucleotide moieties, 3'-3'-inverted abasic moieties, 3'-2'-inverted nucleotide moieties, 3'-2'-inverted abasic moieties, 5'-5'-inverted nucleotide moieties, and 5'-5'-inverted abasic moieties (see columns 3 and 4, for example). Matulic-Adamic et al. teach compositions comprising the nucleic acid and reaction buffer, which is a diluent.

Parrish et al. teach a chemically synthesized siRNA molecule, wherein each strand is 26 bp in length. Additionally, Parrish et al. teach a 742 nt long dsRNA with extensive modification with 2'-deoxy-2'-fluoro modifications, which resulted in successful RNA interference. Parrish teaches that the 2'-deoxy-2'-fluoro modifications incorporated into the long dsRNA produces unc-22 interference and furthermore described the interference as strong (+++, see figure 5).

Crooke teaches gapmer oligonucleotide chemistry and teaches that gapmer strategies increase oligonucleotide affinity to the target RNA (see column 9, for example). Crooke teaches chemical modifications that are incorporated to improve pharmacokinetic binding, absorption, distribution or clearance properties of the compound, affinity or specificity of the compound to target RNA, or modification of the charge of the compound (see column 7, for example).

Crooke teach that a particularly useful 2'-substituent group for increasing the binding affinity is the 2'-fluoro group (see column 12). Crooke also teaches 2'-O-methyl modifications.

It would have been obvious to synthesize a double stranded nucleic acid molecule with the structural characteristics taught by Elbashir et al., wherein the

molecule is formulated in a composition with a diluent, as taught by Matulic-Adamic et al. It would have been obvious to incorporate the specific modifications taught by Parrish et al. and Matulic-Adamic et al.

One would have been motivated to synthesize a double stranded nucleic acid molecule, as taught by Elbashir et al. (EMBO), wherein the molecule is formulated in a composition with a diluent, because Matulic-Adamic et al. teach successful inhibition of target gene expression with nucleic acid molecules formulated in a diluent. Furthermore, the reactions performed by Elbashir et al. require diluents such as buffers and water.

One would have been motivated to synthesize a double stranded nucleic acid molecule, as taught by Elbashir et al. (EMBO), with the modifications taught by Parrish et al. and Matulic-Adamic et al. because each of the modifications were known in the art to protect nucleic acids from exonuclease degradation, which improves the overall effectiveness of the nucleic acid, as well as facilitates uptake of the nucleic acid molecules, as taught by Matulic-Adamic et al. Additionally, Parrish et al. and Matulic-Adamic et al. teach extensive chemical modification of long dsRNA and ribozymes, respectively, with successful inhibition of target gene expression.

Since Elbashir et al. (EMBO), Matulic-Adamic et al., and Parrish et al. teach modified double stranded nucleic acid molecules that inhibit target gene expression, and Crooke teaches gapmer oligonucleotide chemistry to improve pharmacokinetic properties of the oligonucleotide, one would have been motivated to synthesize duplexes, as taught by Elbashir et al., with each of the instantly recited modifications, as

taught by Elbashir et al., Matulic-Adamic et al., and Parrish et al. in order to optimize the activity of the molecule, as taught by Crooke.

Additionally, antisense oligonucleotides, ribozymes, and dsRNAs are each commonly used for sequence-specific mRNA knockdown and each of these encounters delivery problems for effective application. Therefore, one would have been motivated to utilize the same modifications and techniques that have been utilized to overcome these problems with antisense oligonucleotides or ribozymes with siRNAs to add the same benefits to RNAi technology.

For example, Crooke teaches that gapmer oligonucleotide chemistry has provided antisense oligonucleotides with increased target affinity and pharmacokinetic properties. Crooke teaches that different modifications at different regions of the oligonucleotide have been tested in order to optimize oligonucleotide activity. Crooke teaches stepwise experimentation of modifications throughout oligonucleotides in order to find the optimal configuration. Crooke is relied upon as evidence that it is common to experiment with different known modifications at different locations to optimize oligonucleotide activity.

It would have been *prima facie* obvious to perform routine optimization to determine which of the known modifications or combinations of modifications are optimal. As noted in *In re Aller*, 105 USPQ 233 at 235,

More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of the specific modifications used were other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Therefore, one would have been motivated to apply such a method to incorporate known modifications at various locations (i.e. regions/positions of duplex or pyrimidine v. purine) and amounts, as taught by Crooke, into the siRNA duplexes that were synthesized by Elbashir et al.

Finally, one would have a reasonable expectation of success given that each of the modifications were known in the art at the time the invention was made to add benefits to antisense oligonucleotides, ribozymes, dsRNAs or siRNA duplexes, as evidenced by Elbashir et al., Matulic-Adamic et al., Parrish et al. and Crooke, wherein each of the molecules face the same challenges, and each of which can be improved with modifications. Since Crooke teaches effectively walking modifications across antisense oligonucleotides to optimize the location of the modifications and activity of the oligonucleotide and Elbashir et al., Matulic-Adamic et al., and Parrish et al. teach successfully synthesizing modified double stranded nucleic acid molecules, one would reasonably expect for each of the modifications to benefit the double stranded nucleic acid molecules of Elbashir et al. as well. Furthermore, the long chemically modified dsRNA taught by Parrish et al. further demonstrate that extensively modified dsRNA molecules result in RNA interference activity. Since Elbashir et al., Matulic-Adamic et

al., and Parrish et al. teach modification of double stranded nucleic acid molecules and Crooke teaches experimentally determining optimal locations and levels of modification of antisense oligonucleotides, incorporating each of the modifications in the double stranded nucleic acid molecules of Elbashir et al. is considered within the realm of routine optimization.

It is noted that Elbashir et al. teach that 100% modification of one or both strands with 2'-deoxy or 2'-O-methyl modifications abolished activity. However, regardless of the results of these specific modifications at 100% of the positions of one or both strands, Elbashir et al. did modify duplexes and published data regarding successful inhibition with some duplexes and unsuccessful inhibition with others, supporting that testing of such known chemical modifications is routine in the art. The results of Elbashir et al. are considered to offer motivation to incorporate chemical modifications at various percentages to optimize the activity of the duplex because not all modifications result in activity at every percentage.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant argues that although it was known that terminal cap moieties and many chemical modifications can improve the nuclease stability of a nucleic acid inhibitor, whether the stability is compatible with activity must be determined on a molecule-by-

molecule basis. This is consistent with the position of the examiner that routine optimization of known design elements is needed, as explained in the rejection above. Each of the chemical modifications were known in the nucleic acid inhibitor art to impart beneficial stability properties to such nucleic acid inhibitors. Furthermore, it was known in the art that testing/optimization is needed to determine optimal configurations of the modifications within the inhibitory molecules, as evidenced by Elbashir et al. and Crooke. Although applicant asserts that the examiner has cherry picked the modifications from the art, each of the modifications are equally obvious in view of the teachings of the prior art. Furthermore, applicant is not claiming any specific configuration of any specific modifications, but is rather claiming a huge genus of combinations of possible chemical modifications and schematics thereof.

Applicant asserts that the office fails to recognize that a successfully designed siRNA must have stability and activity. This statement is erroneous. The examiner certainly agrees that these two properties are necessary. This is not contradictory to the fact that it would have been obvious to combine chemical modifications that were known in the art to enhance stability of nucleic acid molecules and to optimize the configuration of such to result in active molecules. Elbashir et al. is evidence that incorporation of such chemical modifications into siRNA molecules results in active molecules in some configurations and inactive molecules in others, supporting that routine optimization is needed. Furthermore, Elbashir et al. is evidence that modification is well tolerated in the terminal portions of the duplex, offering further motivation to modify the terminal regions. Elbashir et al. teaches that some modification

does not affect RNAi, but helps to reduce the cost of RNA synthesis and may enhance RNase resistance of siRNA duplexes (see page 6885, column 1).

In addition to Elbashir et al., Crooke is evidence that it was routine in the nucleic acid inhibitor art to incorporate the chemical modifications in different patterns to result in active molecules with improved stability. Therefore, it was known in the art that there must be a balance between improving stability and maintaining a level of activity. Simply because the examiner has set forth that the motivation to incorporate the known modifications is to improve stability does not mean that activity is not a consideration in the routine optimization of placing such modifications. The examiner has not asserted that such modifications should be freely and without limitation incorporated, but rather that it would have been obvious to incorporate the modifications with the motivation of enhancing stability, although it is recognized that optimization is needed to result in active molecules.

Applicant argues that Crooke teaches gapmer patterns, never venturing beyond a single type of modification, 2'-O-methyl, although Crooke clearly had knowledge of a vast number of stabilizing modifications. Crooke is not required to test every possible modification that is known in the art to add stability to nucleic acid molecules to be evidence that it was known in the art to incorporate chemical modifications to enhance stability of nucleic acid inhibitory molecules and that optimization is needed to result in balance between enhancing stability and retaining activity.

Applicant points out that Crooke teaches that it is important not only to pick the right modification(s), but also to position the modifications at the right place because

otherwise the molecule would be inactive. This is completely consistent with the position of the examiner that it was known in the art that optimization of placement/configuration of the modifications is needed and within the grasp of the skilled artisan. In the case of Elbashir et al., Elbashir et al. is silent as to modifications between the terminal regions and the fully modified schematic, wherein fully modified duplexes with 2'-deoxy or 2'-O-methyl modifications abolished activity, supporting again that optimization is needed to determine placement of such modifications for active molecules.

Applicant argues that Parrish et al. teaches that some modifications resulted in instability whereas others were compatible, depending on the location and extent to which the modification was applied, which is again supportive of the instant position that routine optimization is needed to determine the optimal configuration for the instant modifications. Parrish et al. teaches extensive modification of a long dsRNA with 2'-deoxy pyrimidine modifications with resultant interference activity.

Applicant points to *KSR International Co. v. Teleflex Inc.* (127 S. Ct. 1727 (2007)) to argue that the instant claims are directed to a new combination wherein the result cannot be predicted. As explained above, the instant claims are directed to a huge genus of modifications and combinations thereof. One would have been motivated to combine the prior-art elements and expect active molecules within the instant claim breadth. It is well within the grasp of the skilled artisan to select and combine known elements within the instant huge genus and to expect active molecules upon routine optimization of the placement of such modifications given the teachings in the nucleic

acid inhibitor art. It is the routine optimization of the placement of the modifications that is relied upon for determining activity of such molecules, as it was known to perform such routine testing, as evidenced by Elbashir et al. and Crooke.

In view of *KSR International Co. v. Teleflex Inc.*, when a combination of admittedly old elements produces a new and beneficial result never attained before, it is evidence of invention. However, in the instant case applicant is not claiming any specific combination or modification schematic that produces an unexpected result, but is rather claiming a huge genus of possible molecules wherein molecules within the genus are certainly considered obvious in view of the teachings of the prior art.

The mere selection of elements from various prior art references and combining them together with no new function is an obvious use of common sense by one skilled in the art and therefore not patentable.

Furthermore, Elbashir et al. offers motivation to modify terminal nucleotides and Matulic-Adamic et al. teaches the benefit of a plethora of terminal cap moieties and teaches incorporation of such moieties at 5' and/or 3' ends. It is certainly within the realm of routine optimization to incorporate the modifications at one or both of the 5' and 3' ends on each of the strands, as a double stranded nucleic acid molecule only has four possible ends to modify. Additionally, the instant claims do not exclude modification at all four ends but rather only requires the 5' and 3' end of the sense strand. Within instant scope, one would certainly expect for routine optimization to result in active molecules.

One of skill in the art would reasonably expect for the modifications of Matulic-Adamic et al. to likely benefit the molecules of Elbashir et al. as well. As explained above, the motivation need not be the same motivation set forth by applicant, but rather the motivation to enhance the stability of the molecules as set forth by Matulic-Adamic et al. Elbashir et al. teaches that preferred molecules are modified in the terminal regions. Therefore, one would reasonably expect for the terminal cap moieties of Matulic-Adamic et al. to enhance the stability of the molecules of Elbashir et al. as well.

It is noted that the instant broad claim 18 only requires a terminal cap moiety at the 5'- and 3'-ends of the first strand, and an optional 3'-end terminal cap on the second strand. The dependent claims further require one or more of a type of chemical modification. This level of modification would certainly be considered obvious in view of the successful modifications of Elbashir et al. and Parrish et al. combined with the teachings of the instant types of terminal caps of Matulic-Adamic et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thornton*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18-20 and 33-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33-50 of copending Application No. 10/923,536. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to chemically modified double stranded nucleic acid molecules with overlapping structural characteristics and modifications. The instant molecules are not designed to be targeted to any specific target RNA sequence and are therefore obvious in view of the claims of application '536 that recite molecules with overlapping structural characteristics.

Application '536 recites double stranded nucleic acid molecules that comprise a sense and an antisense strand, wherein the antisense region is about 16 to about 25 nucleotides and the sense region is about 3 to about 15 nucleotides in length. Application '536 recites 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, and LNA modifications at varying amounts in one or both strands, as well as terminal cap moieties including inverted deoxy abasic moieties. Application '536 recites terminal cap moieties at the 5'-end, 3'-end or both ends of the sense strand and the 3' end of the antisense strand. Application '536 recites a composition comprising the nucleic acid molecule in a

pharmaceutically acceptable carrier or diluent. Therefore, the instant claims are obvious in view of the claims of application '536.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant argues that the molecules of application '536 are structurally asymmetrical and thus are not obvious variants of the instantly claimed longer molecules. Contrary to applicant's arguments, the claims of application '536 require for the antisense region to be "about" 16 to "about" 25 nucleotides in length and the sense strand to be "about" 3 to "about" 15 nucleotides in length. The "about" 15 language of application '536 certainly embraces 18 nucleotides, the shortest length of the instant claims. Regarding asymmetry between the two strands, the instant claims embrace asymmetric duplexes as well, as the instant claims do not require that each of the strands be identical in length. Therefore, the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY BOWMAN whose telephone number is (571)272-0755. The examiner can normally be reached on Monday-Thursday 6:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AMY BOWMAN
Examiner
Art Unit 1635

/AMY BOWMAN/
Examiner, Art Unit 1635